Citation:

Dey DK, Rothenberg E, Sundh V, Bosaeus I, Steen B. Body mass index, weight change and mortality in the elderly. A 15 y longitudinal population study of 70 y olds. *Eur J Clin Nutr*. 2001;55(6):482-92.

PubMed ID: 11423925

Study Design:

Longitudinal Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The aim of this longitudinal cohort study was to examine:

- the relationship between BMI at age 70 and 15 y all-cause mortality
- the relationship between the percentage of weight change from age 70 to 75 and subsequent 5 and 10 y mortality from age 75
- the BMI range with lowest mortality in representative sample of Swedish elderly.

Inclusion Criteria:

- None clearly listed.
- Three birth cohorts in Gothenburg, Sweden.

Exclusion Criteria:

None listed.

Description of Study Protocol:

Recruitment

- Three birth cohorts: 1901/1902; 1906/1907; 1911/1912.

Design: Longitudinal cohort study

Blinding used: not applicable

Intervention: not applicable

Statistical Analysis

- All analyses were performed separately for males and females.
- Individuals with previously diagnosed cancer at age 70 were excluded from the analyses.
- The Cox proportional hazards regression model was used to determine the risk of dying as a function of BMI together with a number of covariates.
- The dependent variable is 'number of days' from the date of examination at age 70 to the date of death at or before age 85, or the date when one becomes 85-y-old.
- Censored cases were defined as individuals alive at their 85th birthday.
- The exact date of death was obtained from the National registration of the Swedish population.
- Mortality risks were also calculated for three discrete time periods (70-75, 70-80, 70-85) to evaluate possible dependency of such a risk on follow-up period.

BMI and Mortality

- Three different analytical models were used to investigate relative risks (RRs) and the shape of trends (linear and nonlinear) in BMI for mortality.
- In the first set of models, BMI (kg/m^2) values at age 70 were divided into quintiles and used as categorical variable. The RR for mortality and 95% confidence interval (CI) for each BMI quintile were calculated from Cox regression models with birth cohort and smoking habits at age 70 as covariates. The middle BMI quintile was used as the reference group since a U-shaped relationship has been widely reported between BW and mortality by a number of investigators.
- The second set of models was the 'unrestricted quadratic spline model' to determine non-linear trend. In such models, regression lines meet at the interval boundaries to form a smooth curve over the entire range of the variable. A quadratic spline model contains both linear and quadratic terms for the independent variable and was used here to describe the non-monotonic (U- or J-shaped) effect of BMI on mortality. It was done from Cox regression with variables log (BMI), log $(BMI)^2$, four quadratic spline terms and covariates (birth cohort and smoking habits at age 70). The 'knots' or range cut-off points were BMI values at <23, <26 and <28 which resulted in four spline intervals of BMI (< 24, 24-26, 26-28, >28) in both sexes.
- The third set of models was to determine overall linear trends in BMI for mortality risks and was calculated from Cox regression model with log (BMI) and covariates (birth cohort and smoking habits at age 70).
- The differences in log-likelihood ratio between linear model and the spline model was compared to the chi-square distribution with degrees of freedom equivalent to the number of extra parameters in the spline model. This is a formal test of deviation from monotonicity and the significance level is reported as test of non-linear trend. The linear trend was reported only when non-linear trend was not detected by the above-mentioned method.

Covariates

- To adjust the birth cohort effect on the BMI-mortality relation it was used as a covariate in the regression models.
- Smoking habits were divided into three groups: daily smokers at age 70; ex-smokers (previously daily smokers or quitted smoking between age 40-70; and non-smokers (never-smokers or quitted smoking before age 40). These three groups were defined as contrast variable in the model with 'non-smokers' as reference.

Exclusion of Early Deaths

- The RRs for 5 and 10 y mortality in BMI quintiles following age 75 were calculated after exclusion of 310 subjects who died between age 70 and 75.
- The BMI values at age 70 were re-divided into quintiles after exclusion of those deaths and all three analytical models mentioned earlier were used to calculate mortality risks across the quintiles with covariates for birth cohort and smoking habits.

Mortality among Non-smokers

- Cancer cases at or before age 70 were excluded.
- Five, 10 and 15 y mortality risks across the quintiles of BMI in this population were investigated.
- After exclusion of deaths between age 70 and 75 among this non-smoking population, the subsequent 5 and 10 y mortality risks in BMI quintiles were also calculated.
- Analyses were done using all three models with birth cohort as covariate.

Weight Change and Mortality

- The changes in BW were expressed as percentage change in BW between age 70 and 75 y (BW at age 75 minus BW at age 70 divided by BW at age 70 x100) and were divided into five weight change groups: lost >/= 10%; lost 5-9.9%; lost 0-4.9%; gained 0-4.9%; and gained >/= 5%.
- All diagnosed cancer cases at or before age 70 were excluded from the analyses.
- The RR and 95% CI for 5 y (from age 75 to 80 y) and 10 y (from age 75-85) mortality was estimated with covariates for birth cohort and smoking habits at age 70.
- The reference group was weight loss 0-4.9% ('stable weight change group') based on the hypothesis that both extreme weight gain or loss is associated with increased risk for mortality.
- The trends for mortality risks across the weight change groups were determined through Cox regression with 'weight change groups' as continuous variable and, birth cohorts and smoking habits at age 70 as covariates in the model.

Data Collection Summary:

Timing of Measurements

- Cohort I: born 1901/1902; initiated in 1971/1972; followed up regularly to date with 12 examinations in between.
- Cohort II: born 1906/1907; initiated in 1976/1977; followed up with re-examinations at ages 75 and 79.
- Cohort III: born 1911/1912; initiated in 1981/1982; followed up with re-examinations at ages 72, 76 and 86.

Dependent Variables

- Mortality from ages 70 to 75, 70 to 80, and 70 to 85.
- 5, 10 and 15 y mortality

Independent Variables

- BMI: measured in the morning with the subjects wearing light clothing and recorded to the nearest 0.1 kg, and standing height was measured to the nearest centimeter. To minimize methodological inter-cohort differences, all measurements were performed aiming at identical methods by means of, for example, personal contact and training together of the different investigators through-out the studies.

Control Variables

- Birth cohort
- Smoking

Description of Actual Data Sample:

Initial N:

- 2628 (1225 males and 1403 females)
- Cohort I: 1148
- Cohort II: 1281
- Cohort III: 806

Attrition (final N):

- Cohort I: response rate of 85%; 973 (449 males and 524 females)
- Cohort II: participation rate of 81%; 1036 (474 males and 562 females)
- Cohort III: participation rate of 77%; 619 (302 males and 317 females)
- Overall: height and BW data at age 70 available for 2593 subjects (1210 males and 1383 females)
- Three females with BMI values at or above 40 kg/m^2 were excluded from the analysis.
- Individuals with previously diagnosed cancer (77 males and 108 females) at age 70 were excluded from the analyses.

Age: greater than or equal to 70

Ethnicity: study conducted in Sweden

Other relevant demographics:

- The subjects were representative of the community-dwelling elderly and only 2.8% of them were institutionalized.
- The responders of these three cohorts did not differ from the non-responders in respect of sex, martial status and income.
- Some 14.6% of subjects had dependence for both instrumental activities of daily living and personal daily life activities according to the scales defined by Sonn and Asberg; 14.7% of the subjects reported a daily consumption of more than four drugs during the time of examination at age 70.
- The prevalence of diseases at age 70 among the subjects were as follows: cardiovascular diseases 42% (ischemic heart disease 27.6%), stroke 13.7%, cancer 7.1%, diabetes 6.3%, depression 5.6% in a sub-sample of cohort I. Since the majority of subjects were diagnosed with cardiovascular diseases, stroke and diabetes, the authors did a separate analysis to investigate the cause-specific mortality in BMI quintiles at age 70. The authors stated those results would be reported in a separate paper.

Anthropometrics BMI was expressed in quintiles and used as a dependent variable

Location: Sweden

Summary of Results:

Key Findings

BMI and Mortality

- In males, during the 15 y follow-up from age 70 to 85, a non-linear trend was found to be significant for the BMI-mortality relationship where the highest RR (1.20, 95% CI 0.96 - 1.51) was observed in the lowest quintile (14- 22.6 kg/m^2) after adjustment for smoking habits and birth cohort at age 70.
- The lowest mortality risk was found in the middle (reference) quintile (24.7 - 26.4 kg/m^2) for this period of time.
- From age 70 to 75 and 70 to 80, non-linear trends were also found to be significant for males. During these two periods the highest RRs (adjusted) were found to be 1.77 (95% CI 1.13-2.78) and 1.35 (95% CI 1.03-1.79) in the lowest BMI quintiles, respectively.
- In females, a significant non-linear relationship was observed between BMI and mortality risks from age 70 to 75 and 70 to 80.
- The adjusted highest mortality risks for these two periods were 1.63 (95% CI 0.98-2.71) and 1.38 (95% CI 0.96-1.98), and were found in the lowest quintile (14.1 - 22.5 kg/m^2).
- For the total 15 y follow-up, a non-linear trend was also evident for BMI-mortality relation with lowest mortality risk in the middle (reference) quintile (24.6-26.5 kg/m^2).
- The highest mortality risk (1.49, 95% CI 1.14-1.96) during this total 15 y period of follow-up was found in the lowest quintile.

BMI and Mortality after Exclusion of Early Deaths

- After exclusion of subjects who died between age 70 and 75 y, no significant trends or differences were found in the RRs for subsequent 5 and 10 y mortality across the quintiles i both sexes with an exception for males from age 75 -80.
- In females, 10 y mortality risks were 1.52 (95% CI 1.06-2.98) and 1.48 (95% CI 1.03-2.12) in the lowest and highest BMI quintiles, respectively.
- The lowest mortality risks were observed in the middle (reference) quintiles in both sexes.

BMI and Mortality among Non-smokers

- In males there were no significant trends in BMI for 5, 10 and 15 y mortality from age 70.
- The lowest mortality risk (RR=0.96, 95% CI 0.63-1.47) was observed in the fourth quintile (27-29 kg/m ^{2}) after adjustment for birth cohorts.
- In females, during the 5, 10 and 15 yr follow-up periods from age 70, non-linear trends were found to be significant for BMI and mortality relationship.
- For the first 5 y period the highest mortality risk (RR=1.73, 95% CI 0.96-3.11) was observed in the lowest quintile (14.1-22.9 kg/m ^{2}) after adjustment for birth cohorts.
- Higher mortality risks were also found in the lowest BMI quintiles for the following 10 and 15 y follow-up from age 70.
- The lowest mortality risk was observed in the middle (reference) quintile (25-26.9 kg/m^2) during 15 y follow-up from age 70.
- After exclusion of early deaths between age 70 and 75, a non-linear trend was found to be significant in non-smoking males and females for BMI and 10 y mortality from age 75.
- A U-shaped relationship was observed in females where higher mortality risks 1.50 (95% CI

1.03-2.17) and 1.42 (95% CI 1.00-2.00) were observed in the lowest and highest quintiles, respectively for this period of follow-up.

Weight Change and Mortality

- Individuals who lost >/= 10% of their initial body weight between age 70 and 75 had significantly higher mortality risk (males, RR=1.36, 95% CI 0.93-2.00 and females, RR=3.53, 95% CI 1.61-7.74), during the following 5 y period from age 75 compared to the group who lost 0 - 4.9% ('stable' weight change group).
- Ten year mortality risk following age 75 was also significantly higher in both sexes (males, RR=1.62, 95% CI 1.21-2.16; and females, RR=2.15, 95% CI 1.46-3.15) for individuals in this weight-change group.
- Body weight gain of >/= 5% between age 70 and 75 resulted in a numerically lower 5 y mortality risk for the males (RR=0.62, 95% CI 0.38-1.01), and a numerically higher risk for females (2.18, 95% CI 0.95-4.99) of the same weight change group. However, none of them reached statistically significant level.
- The relative risk of 10 y mortality after 75 was found to be lowest among males and females who 'lost 0 - 4.9%' (reference group) of their initial body weight age 70 and 75.

Author Conclusion:

Low BMI and weight loss are risk factors for mortality in the elderly and smoking habits did not significantly modify that relationship. The BMI ranges with lowest risk for 15 y mortality are relatively higher in elderly. Exclusion of early deaths from the analysis modified the weight-mortality relationship in elderly males but not in females.

Reviewer Comments:

Limitations as cited by the authors

- *Did not control for certain clinical and functional conditions such as depression, comorbidity, cognitive and affective status, drug use etc.*
- *Did not control for other chronic diseases as choosing only subjects free from any chronic diseases at age 70 would result in an overselected population.*
- *Since BMI alone does not always capture the joint impact of body composition and body size to health outcomes, further research is needed based on body composition data with certain other variables, e.g. behavioral, social, genetic and environmental, to obtain a clear picture of body weight and mortality relation in the elderly.*

The authors made a statement that 'Since the majority of subjects were diagnosed with cardiovascular diseases, stroke and diabetes we did a separate analysis to investigate the cause-specific mortality in BMI quintiles at age 70.'

May be worthwhile to see if these results have been published and to analyze those findings as well.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions

1.	**Was the research question clearly stated?**		Yes
	1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
	1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
	1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**		Yes
	2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	No
	2.2.	Were criteria applied equally to all study groups?	N/A
	2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
	2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**		Yes
	3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
	3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
	3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
	3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes

	3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
	3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**		Yes
	4.1.	Were follow-up methods described and the same for all groups?	Yes
	4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
	4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
	4.4.	Were reasons for withdrawals similar across groups?	N/A
	4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**		Yes
	5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
	5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
	5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
	5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
	5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**		Yes
	6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
	6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
	6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
	6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes